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THE THYROID GLAND IN RELATION TO HEART DISEASE

The unique function of the cardiovascular apparatus is to supply an adequate quantity of oxygen and nutriments to the tissues. The unique function of the thyroid gland is to produce an internal secretion, the concentration of which determines the metabolic demands of those tissues. It is inevitable therefore that the functional state of the heart and of the thyroid gland are inextricably interrelated: changes in the level of activity of the thyroid gland may be reflected in impressive changes in cardiac dynamics. Indeed many of the cardinal signals of both hyperthyroidism and myxedema arise in the cardiovascular system. Excessive or insufficient thyroid secretion may add an extra burden to an abnormal heart, making clinically manifest or accentuating evidences of heart disease. Accurate assessment of thyroid function in patients with heart disease therefore may be of crucial importance. Simple treatment of some underlying thyroid disease may provide dramatic help for the patient. There have been significant recent advances not only in our concepts of thyroid disease as related to the heart, but also in diagnostic methods and therapeutic resources.

MASKED THYROTOXICOSIS

The day is nearly past when one encounters with any frequency a patient with florid thyrotoxicosis, with staring eyes, a large goiter, disordered cardiac rhythm, and congestive heart failure. The present day problem is rather the determination of whether a mild over-activity of the thyroid gland is providing an excessive load on a heart already encumbered with impaired blood supply or valvular deformity. The thyrotoxicosis may not be evident at first inspection, but may be so well masked as to be missed entirely. It may arise either from an old multinodular goiter, from a single toxic nodule, or from a diffusely hyperplastic gland.

Nodular Goiter: A masking of thyrotoxicosis by dominating cardiac symptoms appears to be particularly a problem in patients who have for years carried a multinodular goiter. A large percentage of these glands begin to secrete an excessive amount of hormone in the fifth, sixth and later decades. The changes are extremely slow and subtle. A slight excess of thyroid hormone acting over a period of years will severely tax the heart. Only if there is awareness on the physician's part of the possibility of hyperthyroidism will such a patient receive proper care.

The historical and physical findings which suggest mild toxicity are often familiar ones, such as an excessive appetite or excessive sweating, but the disease may be suggested only casually and incidentally. One of our associates recently suspected thyrotoxicosis (subsequently proven) because the feet of an elderly patient seemed too warm. Another of our patients first visited the orthopedic clinic for pain and weakness of his thighs, a not unusual manifestation of the muscular wasting of thyrotoxicosis. Auricular fibrillation which fails to respond to full doses of digitalis, frequent premature beats, otherwise unexplained tachycardia, and recurrent ectopic rhythms are suggestive of thyrotoxicosis. Diagnosis may prove difficult, for the classic features of the disease may be barely perceptible, entirely missing, or obscured by the manifestations of the heart disease. An increased appetite may give way to anorexia when congestive heart failure occurs. On the other hand, congestive failure alone may mimic thyrotoxicosis. Some degree of heat intolerance and tachy-

cardia may be seen, and dyspnea elevates the basal metabolic rate. If the diagnosis is suspected but not evident, one must rely on objective measures of thyroid function. The time-honored test is the basal metabolic rate, but this may be normal in patients with thyrotoxicosis or high in patients without thyroid disease who are emotionally disturbed.

The simplest objective test of thyroid activity is the radioactive iodine (I^{131}) test. It is without risk or discomfort to the patient, and is usually reliable, and informative. It is of no value if the patient has been taking iodide in any form in the recent past or if he has received any of the iodinated contrast media such as are used for the visualization of the gall bladder, subarachnoid space or bronchial tree. The results of the determination are given in terms of the percentage of the administered dose retained in the thyroid at an arbitrary time, usually 24 or 48 hours after the test dose was given. In our laboratory values over 50% retention are viewed with suspicion and those over 60% are considered almost diagnostic of thyrotoxicosis.

The determination of the protein-bound iodine of the blood is another valuable diagnostic adjunct. This is a rather difficult laboratory procedure but of great value if accurately done. The normal range is between 3.5 and 8 micrograms per 100cc of plasma. Higher values are indicative of thyrotoxicosis. The ingestion of large doses of iodide over a period of several weeks or longer may elevate the reading, as will administration of any of the iodinated dyes.

It is worth remembering that these various tests measure different things. The basal metabolic rate measures the rate at which the body is using oxygen. The I^{131} accumulation measures the rate of activity of the thyroid gland in trapping iodides. The PBI of the blood is an index of the concentration of calorigenic hormone in the peripheral blood. Usually these indices are interrelated, but at times dissociations occur which are puzzling. Nevertheless it seems wisest wherever the diagnosis is in doubt to have all three values in order that assessment of the patient may be as complete as possible.

Graves' disease: The foregoing remarks have pertained primarily to multinodular toxic goiter associated with heart disease. They apply with almost equal force to heart disease complicating or complicated by toxic diffuse goiter (Graves' disease). Here the diagnosis may be equally difficult especially in the male; or when the goiter is small or very low-lying or substernal; or in patients with short thick necks. It is our impression that Graves' disease has a more explosive course than multinodular goiter, and that accordingly the thyrotoxic aspects of the disease are more evident. One must remember, however, that there is no sharp dividing line between the normal state and the thyrotoxic one. It is the borderline states that create the greatest difficulty. Even the most refined of our present day laboratory aides may fail of a definite answer. What is the wisest policy to persue in such a case? One may wait further developments; or one may arbitrarily assume a diagnosis and treat accordingly; or one may employ iodide or an antithyroid drug as a therapeutic-diagnostic trial. This last is more commonly confusing than helpful, but in an occasional situation will give a definitive answer.

TREATMENT:

The clinical facts and the laboratory tests form the basic information on which a diagnosis of thyrotoxicosis may be made. It is then necessary to proceed with treatment. There are three choices: thyroidectomy after suitable preparation, radioactive iodide, and the chronic administration of an antithyroid drug such a propyl thiouracil. The relative values and risks of these three forms of treatment have been carefully reviewed recently[1]. The choice may be dictated by the conditions at hand. Thus the severity of the heart disease may preclude surgery, or recent ingestion of iodide may deny the early use of therapeutic I^{131}. At the Thyroid Clinic of the Massachusetts General Hospital I^{131} has not been routinely used in treatment of multinodular goiter with thyrotoxicosis because of the possibility that such glands might be sites of malignant disease. This relatively small risk, however, is to be compared with the alternative risk of surgery. One unfortunate finding of malignant change a few months after I^{131} therapy has perhaps influenced us unduly, but there is now a trend to increase the use of I^{131} in nodular goiter. One other problem to be kept in mind is that in general multinodular glands respond more slowly to the isotope than do glands with diffuse hyperplasia. The use of this therapy may therefore result in considerable delay in restoration of the euthyroid state. Our experience has been that chronic use of antithyroid drugs is inadequate therapy.

THYROTOXICOSIS COMPLICATING HEART DISEASE

Patients with heart disease are as prone to develop thyroid disease as are others, but when they do, the situation is more dangerous and the therapeutic indications are different. This subject has recently been carefully studied by Maloof and Chapman[2] who reported on 47 patients with hyperthyroidism with predominant cardiac manifestations. These patients were treated with I^{131}. Twenty-seven had auricular fibrillation, 25 congestive failure, and 16 both. In 12 the fibrillation disappeared after treatment. Most of these patients responded to a single dose of the isotope, but a few required a second or a third dose. There seems to be no question but that these patients responded in a satisfactory fashion to I^{131}. The only major problem is that at times the response is slow. Maloof and Chapman did not observe an aggravation of the heart disease during the post-treatment period, when at times a distinct rise in the protein-bound iodine content of the serum was observed. It seems probable that this rise is in large part comprised of non-calorigenic products of radiation necrosis of the gland.

THYROIDECTOMY FOR HEART DISEASE

Approximately 2 decades ago total thyroidectomy had a transient vogue in the treatment of patients without thyrotoxicosis but with severe angina pectoris or congestive heart failure. The pioneers of this approach were Cutler and Blumgart and their associates. The slowed circulation of patients with myxedema suggested that the induction of myxedema artificially might lighten the demands on a diseased and inadequate heart and permit restoration of competence or relative adequacy of coronary flow. Several hundred total thyroidectomies were done. Disregarding an operative mortality of approximately 10% the results were often surprisingly good. Many patients were able to resume productive lives and to live comfortably. It is only fair to say that the results obtained varied widely from clinic to clinic, a phenomenon perhaps explained in part by variations in selection of patients. It would be extremely helpful to have a final evaulation of results obtained in this group of patients from one of the clinics which was actively engaged in the project in the 1930's. The procedure was abandoned because of the high mortality and morbidity. The parathyroprivia which so often accompanied the total thyroidectomy was particularly troublesome.

Thyroid ablation has been revived during the past few years with the ready availability of I^{131}. The results again are arresting. The isotope has the advantage over surgical thyroidectomy in that there is no operative discomfort, complication, or mortality. The procedure is inexpensive and simple. The majority can be rendered hypothyroid or myxedematous with a single dose, although it may take many weeks before the full effectiveness of the isotope is reached. Because of variations in radiation sensitivity, size, and uptake of glands it is impossible to judge the dose precisely. There is a difference of opinion regarding the result to be achieved. Some attempt to estimate a dose which will make the patient hypothyroid but not myxedematous, whereas others prefer to give a dose calculated to produce full myxedema, and then control the unpleasant symptoms of myxedema with small doses of disiccated thyroid. Because of the difficulty in calculating dosage and the unpredictability of response, the latter course seems more logical and expedient. The dose of I^{131} usually required to produce myxedema is about 35 millicuries. No adverse effects on the bone marrow have been seen with this quantity of the isotope.

Blumgart and his associates[3] have recently described the type of patient most suited to this form of therapy. He or she is a person between the ages of 40 and 60 with angina pectoris of more than a year's duration which has been disabling and unresponsive to the most intensive medical measures. One or more myocardial infarctions may have occurred. The blood pressure is normal or nearly so and the basal metabolic rate is not already depressed. Blumgart expects that well over half of such patients may experience considerable relief of angina pectoris following I^{131} ablation of their normal gland. Less satisfactory results may be expected in congestive heart failure.

Much remains to be learned both as to the technic of I^{131} therapy and especially in the selection of patients, but there seems little doubt that symptomatic benefit can be expected from the ablation of the normal thyroid glands of many patients with heart disease uncontrolled by more conventional forms of therapy. The relief may be well in excess of the discomfort caused by the hypo-

thyroidism. Present information is inadequate to answer with certainty whether life is prolonged or shortened. The latter possibility has been broached by those who question the wisdom of a procedure which may elevate the blood cholesterol in a patient already suffering from arteriosclerosis.

MYXEDEMA AND THE HEART

Patients with myxedema have long been known to have severe atherosclerosis of the major vessels and especially of the coronary arteries. It is not yet known whether the coincidental hypercholesteremia is responsible. These patients may be in excellent adjustment to the impaired coronary flow because the heart rate is slow, the cardiac output, small; and the work of the heart, reduced. If, however, by administering thyroid the work of the heart is increased, the coronary flow may be inadequate, and the angina pectoris can be precipitated by such therapy. It is for this reason that it is wisest to begin treatment of myxedema in the elderly with small doses, e.g., 15 milligrams daily, slowly increasing by increments of 15 milligrams every two to four weeks until a satisfactory dose level is reached, or until symptoms of cardiac embarrassment occur. It will often be found that 30 to 60 milligrams of thyroid is adequate to control the more unpleasant symptoms of myxedema in the elderly, while larger doses give the patient precordial distress upon effort. A rare patient is so delicately poised that even a minute dose of thyroid is not tolerated. However, perhaps because of the formation of new collaterals and consequent improvement of coronary flow, it is often times possible to increase thyroid medication after a period to a level which had previously given heart symptoms.

SUMMARY

Thyrotoxicosis, either overt or masked, may produce or accentuate pre-existing heart disease. Determination of the protein-bound iodine of the serum and assay of the radioactive iodine accumulation by the gland may be invaluable in clinching a diagnosis of hyperthyroidism. Oftentimes radioactive iodine is the treatment of choice for such patients.

For certain selected patients with intractable angina pectoris or congestive heart failure radioactive iodine ablation of the normal thyroid may be of value.

Patients with myxedema may respond to administration of desiccated thyroid with an alarming increase in heart symptoms. For this reason caution is necessary in the dose of thyroid given to elderly myxedematous subjects.

John B. Stanbury,
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EIGHTH INTERNATIONAL CONGRESS OF SURGERY

Members of the American Heart Association are invited to attend the Eighth International Congress of Surgery which is to be held in Madrid, Spain, from May 19 to May 24, *1952*. One of the features of the Congress is a program on vascular surgery, sponsored by the Section on Vascular Surgery. The program of the sections will be augmented by scientific exhibits and by a number of visitations to the many famous landmarks of Madrid. Information may be obtained from the Secretary of the Congress at the National Institute of Medicine and Surgery, University of Madrid, Madrid, Spain.

THE IV INTERAMERICAN CARDIOLOGICAL CONGRESS

The IV Interamerican Cardiological Congress is to be held in Buenos Aires from September 1-6, 1952, under the auspices of the Argentine Society of Cardiology with Doctor Pedro Cossio as President of the Congress.

FIRST EUROPEAN CONGRESS OF CARDIOLOGY

A European Congress of Cardiology will be held in London, September 10 to 12, *1952*. The Congress is being organized by the British Cardiac Society with Sir John Parkinson, Chairman. Membership will be open to all member societies affiliated with the European Society of Cardiology. Non-members may attend Scientific Sessions by invitation of the Organizing Committee. Titles and short abstracts of communications should be sent by contributors to the Secretaries of their national Cardiological Societies. For further details write to: the Secretary of the European Congress of Cardiology, The Institute of Cardiology, 35 Wimpole Street, London, W. 1.